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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/069,663	02/27/2002	A. K. Gunnar Aberg	559P017	3512
42754	7590	08/04/2006	EXAMINER	
NIELDS & LEMACK 176 EAST MAIN STREET, SUITE 7 WESTBORO, MA 01581			CHANG, CELIA C	
			ART UNIT	PAPER NUMBER
			1625	

DATE MAILED: 08/04/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

10/069,663

Applicant(s)

ABERG ET AL.

Examiner

Celia Chang

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 19 June 2006.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1,6-10,13-15,18,19,21 and 22 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 6 is/are allowed.
- 6) ☒ Claim(s) 1,7-10,13-15,18,19,21 and 22 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- ☒ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_.
- ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: \_\_\_\_\_.

### DETAILED ACTION

1. This application is a RCE of SN 10/069,663.

Amended claims 1, 6-10, 13-15, 18-19, 21-22 are pending. Prosecution continues for the currently amended claims.

2. The rejection of claims 1, 7-10, 13-15, 18-19 and 21 under 35 USC 112 second paragraph is dropped in view of the amendment deleting the term "a metabolite of ketotifen."

3. The rejection of claims 1, 7-10, 13-15, 18-19 under 35 USC 112 first paragraph is dropped in view of the current amendment limiting to S-isomer substantially free from the R-isomer of compounds of formula I wherein R is H i.e. an optical purity.

The rejection for broad scope of allergic disorders etc. is dropped in view of the amendment wherein the disorders have been limited to those against which ketotifen has therapeutic activity, because the specification described that norketotifen have similar activity as ketotifen being the active metabolite of ketotifen.

4. The rejection of claims 1, 7-10, 13-15, 18-19 and 21 under 35 USC 103(a) over Aberg I or II in view of Polivka I or Polivka II is maintained for reason of record and further applied to claim 22.

Applicants argued that just because ketotifen was separated into pure S or R isomers does not render the instant metabolite obvious since separation of norketotifen must be accomplished on its own. This is not persuasive. Please note that in so far as the compound is concerned, the biological system is well recognize to maintain stereo selectivity in its process (see per ponderous ref. EMBASE 1985022681, 1986195020, 1991318244), therefore in possession of the pure S-ketotifen i.e. Pilivka I, one skilled in the art would expect to obtain the "S" metabolite without substantial "R" isomer, i.e. the S-norketotifen of the instant claims. There is no good reason that when a subject is given pure S-ketotifen would metabolized it into a mixture of S and R norketotifen thus the purity of the compound becomes different. Applicants' attention is

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drawn to that non-biological synthesis process i.e. claim 6, was not under rejection. Please also note that a product by process claim is a "product" (See MPEP 2113).

Attorney further argued that the metabolite has less side effect than the parent ketotifen. Such argument provided little probative value without support by factual evidence. Especially, it is noted on page 3 of the specification, it is well recognized that "*it was found that while both isomers of ketotifen had approximately the same antihistaminic activity, almost all the sedative sideeffects were found to reside in R(+)-ketotifen*". Many drugs have active metabolites (see Garattini, p. 219) however, an allegation of administering metabolite free from the parent drug will have different toxicity or side effect must be supported by factual basis. The specification provided clear statement that, in so far as the "S" ketotifen is concerned, side effect is not an issue. Especially, the pure "S" ketotifen was available without CNS side effect i.e. Pilivka I. Applicants provided no evidence or comparative value as to when the "substantially pure S" metabolite of the claims was administered independently of the parent drug, i.e. pure S-ketotifen of Pilivka I, would have any difference in side effects. Any advantage between racemic ketotifen and racemic norketotifen has no relevancy over the instant claims. Attorney's allegation without competent factual support is entitled to little weight. In re Lindner 173 USPQ 356.

5. Claims 6 is allowed.

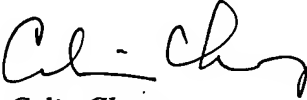
6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celia Chang whose telephone number is 571-272-0679. The examiner can normally be reached on Monday through Thursday from 8:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thomas McKenzie, Ph. D., can be reached on 571-272-0670. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

*OACS/Chang*  
*July 31, 2006*

  
*Celia Chang*  
*Primary Examiner*  
*Art Unit 1625*